IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Re: Appeal to the Board of Patent Appeals and Interferences

Appellants	MacDonald et al.	Examiner:	Nathan W. Schlientz
Serial Number:	10/731,256	Group Art Unit:	1616
Filed:	December 9, 2003	Customer Number:	22827
Confirmation No:	4720	Deposit Account:	04-1403
Title:	Triggerable Delivery System for Pharmaceutical and Nutritional Compounds and Method of Utilizing Same	Attorney Docket No.	KCX-859 (19100)

1. ☐ **NOTICE OF APPEAL**: Pursuant to 37 CFR 41.31, Applicant hereby appeals to the Board of Appeals from the decision dated _____ of the Examiner twice/finally rejecting claims _____.

2. ☒ **BRIEF** on appeal in this application pursuant to 37 CFR 41.37 is transmitted herewith (1 copy).

3. ☐ An **ORAL HEARING** is respectfully requested under 37 CFR 41.47 (due within two months after Examiner's Answer).

4. ☐ Reply Brief under 37 CFR 41.41(b) is transmitted herewith (1 copy).

5. ☐ "Small entity" verified statement filed: [ ] herewith [ ] previously.

6. **FEE CALCULATION:**

	Fees
If box 1 above is X'd enter $ 540.00	$ 0.00
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PETITION is hereby made to extend the original due date of March 7, 2009, hereby made for an extension to cover the date this response is filed for which the requisite fee is enclosed (1 month $130; 2 months $490; 3 months $1,110; 4 months $1,730, 5 months $2,350 $ 0.00

SUBTOTAL: $ 540.00

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Less any previous fee paid for prior Notice of Appeal since Board did not render a decision on the merits. MPEP § 1204.01 - $ 0.00

Less any previous fee paid for submitting Brief on prior Appeal since Board did not render a decision on the merits. MPEP § 1204.01 - $ 0.00

SUBTOTAL: $ 540.00

If "small entity" verified statement filed ☐ previously,
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☐ Fee NOT required since paid in prior appeal in which the Board of Appeals did not render a decision on the merits.

The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any fees in addition to the fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (deficiency only) now or hereafter relative to this application and the resulting official document under Rule 20, or credit any overpayment, to our Account No. shown in the heading hereof. This statement does not authorize charge of the issue fee in this case.

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I hereby certify that this correspondence and all attachments and any fee(s) are being electronically transmitted via the internet to the U.S. Patent and Trademark Office using the Electronic Patent Filing System on February 23, 2009.

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PATENT
ATTORNEY DOCKET NO: KCX-859 (19100)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application: MacDonald et al.	)	Examiner: Nathan W. Schlientz
Serial No: 10/731,256	)	Group Art Unit: 1616
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Commissioner for Patents
P.O. Box 1450
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BRIEF ON APPEAL

Appellants submit the following brief on appeal in accordance with 37 C.F.R. § 41.37:

1. REAL PARTY IN INTEREST

The real party in interest in this matter is the assignee of record, Kimberly-Clark Worldwide, Inc.

2. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to the Appellants or the Appellants' legal representative which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

3. STATUS OF CLAIMS

Currently, claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, and 62-67 remain pending in the present application including independent claim 28. Claims 1-27, 29, 32, 36, 39, 41, 45, and 47-61 were previously cancelled from the present application. Claims 66 and 67 are presently withdrawn as there is currently no allowed generic claim. All pending claims are attached hereto in the Claims Appendix.

In the Final Office Action of September 5, 2008, claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, 64 and 65 were finally rejected under 35 U.S.C. § 103(a). Claims 62 and 63 were finally rejected under 35 U.S.C. § 112, first paragraph.

The rejection of claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, and 62-65 is hereby appealed.

4. STATUS OF AMENDMENTS

All amendments have been entered into the record.

5. SUMMARY OF CLAIMED SUBJECT MATTER

In general, the present application is directed to a triggerable delivery system for pharmaceutical and nutritional compounds. See, e.g., Title. For example, independent claim 28 is directed to a method for using a triggerably releasable delivery system. See, e.g., pg. 2, line 16 – pg. 3, line 10. The method includes administering a plurality of nanoparticles containing silica coated with alumina to a mucosal membrane of a patient. See, e.g., pg. 4, lines 15-24. The nanoparticles have a size of about 500 nanometers or less. See, e.g., pg. 19, lines 20-21. The alumina provides a site on a surface of the nanoparticles to which is bonded a functional compound. See, e.g., pg. 5, lines 18-19. The nanoparticles possess a zeta potential of about 20 millivolts or more. See, e.g., pg.

7, lines 22-26. A vehicle that comprises a pH altering material contains the nanoparticles. See, e.g., pg. 16, lines 1-16. The functional compound is released from the surface of the nanoparticles upon exposure to a change in pH. See, e.g., pg. 2, line 30 – pg. 3, line 2.

Claim 65 adds the limitation to independent claim 28 that the functional compound includes tetracycline. See, e.g., pg. 9, line 23 – pg. 10, line 12.

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Claims 62 and 63 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

II. Claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, 64 and 65 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over International Application No. WO 03/032959 (hereinafter "Bosch") in view of U.S. Patent No. 5,597,575 (hereinafter "Breitbarth") and "Fundamentals of Adsorption" to Ma, as evidenced by "Aggregation and Photophysics of rose Bengal in Alumina-Coated Colloidal Suspensions" (hereinafter "Daraio").[1]

III. Claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, 64 and 65 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,548,264 (hereinafter "Tan") in view of Bosch and Ma as evidenced by Daraio.

7. ARGUMENT

Appellants respectfully submit that the presently pending claims are patentable over the cited references and rejections.

[1] The Final Office Action included a second rejection of all pending claims based on the same combination of the references. The second rejection appears to be a replica of the first rejection with no new comments. As such, Appellants submit that the arguments below in response to this rejection additionally apply to the replica rejection citing Bosch, Breitbarth, Ma, and Daraio in combination.

I. Claims 62 and 63 comply with the written description requirement under 35 U.S.C. § 112.

To satisfy the written description requirement, a patent specification must describe an invention in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed subject matter," to ensure, e.g., that the inventor had possession of the claimed subject matter as of the desired priority date. Lockwood v. American Airlines, Inc., 41 USPQ2d 1961 (Fed. Cir. 1997); In re Gostelli, 10 USPQ2d 1614 (Fed. Cir. 1989). Thus, the specification need only convey to those skilled in the art with reasonable clarity that Applicants possessed the claimed invention. Importantly, the subject matter of the claim need not be described literally (i.e., using the same terms). *See* M.P.E.P. § 2163.02.

Claim 62 adds the limitation that the pH altering material includes an acid. Claim 63 adds the limitation that the pH altering material includes a base. The Final Office Action alleges that:

> the instant specification does not provide for the pH altering material including an acid or a base, but only provides support for the pH altering material including carbonates, bicarbonates and buffering salts which would result in a pH change on becoming wet with water or biological fluid.

Appellants respectfully disagree. The present specification discloses:

> By the use of a "pH trigger" the functional compounds can be released in a controlled manner when needed. It should be noted that such triggering of the delivery system may be accomplished through environmental changes such as infection which results in pH changes, taking advantage of inherent differences in pH depending on body locations, and the intentional act of introducing chemistries such as pH altering materials to the delivery systems to trigger the release of functional compounds. Pg. 16, lines 3-9.

Thus, the "pH trigger" can be accomplished utilizing a pH altering material in the delivery system. Appellants disclose extensively that acids or bases can be utilized to

"trigger" the release. For instance, regarding an acid, Appellants disclose that "the pH triggered release for silica coated particles is activated by adding acid and lowering the pH to the environment of the silica particles." Pg. 16, lines 22-23. Regarding a base, Appellants disclose that "by changing the pH of the modified nanoparticle suspension to high pH values, the pharmaceutical agent was released . . . in particular, the alkaline agent, dilute sodium hydroxide[2] (0.1 N), was added in 0.5 ml amounts to the samples." As such, Appellants respectfully assert that the use of an acid or base as a pH altering material is adequately disclosed in the specification to satisfy the written description requirement of § 112.

Secondly, even **if** Appellants did not explicitly disclose that the pH altering material could be an acid or a base, Appellants submit that it is inherently disclosed in the specification. As noted above, Appellants disclose numerous times the use of acids and bases to alter pH to trigger the release of the compound. Furthermore, one of ordinary skill in the art would reasonably conclude that a pH altering material could be an acid or a base. One of ordinary skill in the art understands that a primary means of pH altering in chemistry is accomplished by the addition of an acid or a base. As such, Appellants respectfully submit that the inventors were clearly "in possession" of utilizing an acid or a base as a pH altering material at the time of filing.

[2] One of ordinary skill in the art understands that sodium hydroxide is a strong chemical base that is widely used in industry.

II. Claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, 64 and 65 are patentable over Bosch in view of Breitbarth and Ma, as evidenced by Daraio.

Bosch is directed to nanoparticulate compositions comprising inorganic cores. The inorganic cores may be coated with pharmaceutically active agents to produce stable dispersions.

Breitbarth is directed to compositions for stimulating hair growth. The compositions include a non-metallic carrier coated with vitamin D_3. The carrier can be macroparticulate silica particles having a mean particle diameter of >40 microns, microparticulate silica particles having a mean particle diameter between 3 and 10 microns, or alumina microparticles with an average particle size of about 7 microns.

Ma is directed to adsorption of proteins and antibiotics on alumina membranes during filtration. Ma et al. indicates that the amount adsorbed is dependent upon pH.

Daraio is cited as evidence that Nalco 1056 is alumina coated silica nanoparticles.[3]

A. Independent claim 28 is patentable over Bosch in view of Breitbarth, Ma, and Daraio.

Independent claim 28 recites:

> A method of utilizing a triggerably releasable delivery system, the method comprising administering to a mucosal membrane of a patient a plurality of nanoparticles containing silica coated with alumina and having a size of about 500 nanometers or less, wherein the alumina provides a site on a surface of the nanoparticles to which is bonded a functional compound, wherein the nanoparticles possess a zeta potential of about 20 millivolts or more, **wherein the nanoparticles are contained within a vehicle that further comprises a pH altering material, and wherein the**

[3] Appellants are unsure of the purpose of Daraio. It is stated that Daraio provides evidence that Nalco 1056 is alumina coated silica. Bosch, however, does not disclose the use of Nalco 1056. In contrast, Bosch discloses the use of Nalco particles with an alumina core (i.e., not a silica core coated with alumina). See, e.g., pg. 27, lines 28-29; pg. 34, lines 9-10 and lines 14-15; and pg. 35, lines 19-20.

functional compound is released from the surface of the nanoparticles upon exposure to a change in pH.

1. Bosch, Breitbarth, Ma, and Daraio fail to teach or suggest nanoparticles contained within a vehicle that further comprises a pH altering material.

To establish a *prima facie* case of obviousness, in addition to other requirements, the prior art references when combined must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). As noted above, independent claim 28 contains the limitation that the nanoparticles are contained within a vehicle that further comprises a pH altering material. Appellants disclose that "triggering of the delivery system may be accomplished . . . (by) the intentional act of introducing chemistries such as pH altering materials to the delivery systems to trigger the release of the functional compounds." Pg. 16, lines 4-9. None of the references teach or suggest this limitation.

In Appellants' Amendment dated March 17, 2008, Appellants introduced the limitation that the nanoparticles are contained within a vehicle that further comprises a pH altering material. In response, the Final Office Action failed to address this limitation. Appellants filed a Request for Reconsideration dated December 5, 2008 and again argued that none of the references either alone or in combination obviated nanoparticles contained within a vehicle that further comprises a pH altering material. In the Advisory Action dated December 18, 2008, the Office again failed to address this limitation. Appellants note that "[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 165 USPQ 494, 496 (CCPA 1970). As such, Appellants submit that independent claim 28 defines over the references either alone or in proper combination.

2. The Examiner improperly combines the teachings of Bosch with Breitbarth.

In rejecting claims under 35 U.S.C. § 103, it is incumbent upon the Examiner to establish a factual basis to support the legal conclusion of obviousness. See In re Fine, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). "[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a prima facie case of unpatentability." In re Oetiker, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Furthermore, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007) (quoting In re Kahn, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). Accordingly, even if all elements of a claim are disclosed in various prior art references, the claimed invention taken as a whole cannot be said to be obvious without some reason given in the prior art why one of ordinary skill would have been prompted to modify the teachings of the references to arrive at the claimed invention. See e.g., In re Regel, 188 U.S.P.Q. 132 (C.C.P.A. 1975).

Applicants note that one of ordinary skill in the art would not seek to combine the references in the manner taught in the Office Action. As noted above, Bosch teaches nanoparticulate compositions comprising inorganic cores coated with pharmaceutically active agents. Bosch teaches that the inorganic cores have particles size of less than 1 micron. Pg. 10, line 15. Additionally, Appellants claim nanoparticles having a particle size of about 500 nanometers or less. Furthermore, Appellants claim administering the nanoparticles to a mucosal membrane. Appellants also claim that the nanoparticles possess a zeta potential of about 20 mV or more.

In stark contrast to Bosch and Appellants' claims, Breitbarth discloses silica carriers with a minimum size of 3 microns (which is approximately **six times** the size of Applicants' claimed maximum **nanoparticle** size) and alumina carriers having an average particle size of about 7 microns (approximately **fourteen times** the size of Applicants' claimed maximum **nanoparticle** size.) Col. 2, lines 40-56. Additionally, Breitbarth discloses a desire for microparticles with a negative surface charge. See claims 1, 16, and col. 2, lines 36-39. As noted above, Applicants claim nanoparticles with a zeta potential of +20 millivolts or more. Finally, Breitbarth is not directed to application to mucosal membranes. By distinction, Breitbarth is directed to a composition for stimulating hair growth. See Title.

As such, Breitbarth clearly **teaches away** from Appellants' claimed invention. Only with Appellants' specification could the structure of claim 28 be attained, and any attempt to arrive at the structure of claim 28 through study of the cited references is only reachable from improper hindsight analysis after viewing Applicants' specification.

In the Advisory Action of December 18, 2008, the Examiner responds to Appellants' arguments of improper combination stating "Breitbarth is cited to show the state of the art at the time of the instant invention."

Appellant emphasizes that the teachings of the references must be viewed in their entirety, i.e., as a whole, to sustain a *prima facie* case of obviousness under 35 U.S.C. §103(a). Further, the appropriate test under 35 U.S.C. §103(a) is not whether the differences between the prior art and the claims are obvious, but instead whether the claimed invention as a whole would have been obvious. That is, the differences between a particular claim and the cited references cannot be viewed in a vacuum.

Appellants respectfully submit that the Examiner has failed to point to any disclosure that would obviate applying **nanoparticles** with a zeta potential of **+20 mV or more** and a functional compound bonded thereto to a **mucosal membrane** wherein the functional compound is released from the surface of the nanoparticles upon exposure to a change in pH. Thus, Appellants respectfully submit that the Examiner's purported combination simply picks and chooses just those components needed from a prior art reference to combine in a § 103 combination without regard to the entirety of the disclosures of the references. As such, Appellants respectfully submit that the resulting combination is improper.

B. Dependent claim 65 is patentable over Bosch in view of Breitbarth, Ma, and Daraio.

Claim 65 adds the limitation that the functional compound includes tetracycline. In attempting to obviate this limitation, the Examiner cites Ma as disclosing releasing tetracycline from the surface of nanoparticles upon exposure to a change in pH. Applicants respectfully note, however, that Ma is directed to adsorption of proteins and antibiotics on alumina membranes during filtration. Ma simply indicates that the amount adsorbed is dependent upon pH. Ma does **not** teach that after adsorption onto the alumina membranes, a change in pH forces the release of the compound from the surface. Simply because Ma discloses that the amount adsorbed is a function of pH, it can not be said that Ma obviates releasing tetracycline from the surface upon exposure to a change in pH.

Additionally, Appellants submit that the Examiner has again scoured the prior art and simply "picked" the tetracycline from Ma and attempted to combine with the base combination. As noted above, Ma discloses a filtration process. One skilled in the art

would not take the teachings of Ma and attempt to construct Appellants' invention without utilizing Appellants' claims as the sole motivation. Such a combination relies on impermissible hindsight in constructing Appellants' invention out of the isolated teachings of the prior art.

III. Claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, 64 and 65 are patentable over Tan in view of Bosch and Breitbarth and Ma, as evidenced by Daraio.

Tan describes core-shell nanoparticles in which the core may be a magnetic material (e.g., magnetite), metal or metal salt (e.g., gold), and so forth, and the shell may be silica or alumina.

A. Independent claim 28 is patentable over Tan in view of Bosch, Breitbarth, Ma, and Daraio.

Tan is cited as allegedly disclosing Appellants' claimed nanoparticles containing silica coated with alumina.

1. Contrary to that alleged in the Final Office Action, Tan fails to teach nanoparticles containing silica coated with alumina.

To establish a *prima facie* case of obviousness, in addition to other requirements, the prior art references when combined must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Appellants respectfully submit that while Tan may generally described alumina- or silica-coated nanoparticles, however, it does not disclose or suggest the claimed alumina-coated *silica nanoparticles*.

In order to yield this limitation, the Office Action points to an excerpt of Tan that states that the shell can include a first layer of silica coating immediately adjacent to the core and a second layer coating the silica layer. The Office Action states "it would have

been *prima facie* obvious for one skilled in the art . . . to make the nanoparticles of Tan et al. . . . wherein the shell comprises silica coated with alumina, as reasonably taught by Tan et al." Appellants respectfully disagree. The only mention of a second layer in Tan discloses that:

> the second layer can be composed of a biodegradable material (e.g., a sugar or polymer) impregnated with a drug. When introduced to an animal, the biodegradable material and drug will gradually be dissolved into the animal. Col. 6, lines 4-8.

Thus, Tan does not reasonably teach silica coated with alumina. Furthermore, Tan discloses that the shell may be composed of alumina or silica (among other potential components). Tan does not obviate coating alumina onto silica nanoparticles to one of ordinary skill in the art.

2. Tan, Bosch, Breitbarth, Ma, and Daraio fail to teach or suggest nanoparticles contained within a vehicle that further comprises a pH altering material.

Appellants respectfully submit that Bosch, Breitbarth, Ma, and Daraio fail to disclose or suggest Appellants claimed limitation of nanoparticles contained within a vehicle that further comprises a pH altering material for the reasons noted above in section II.(A.)(1.). Tan fails to remedy this deficiency. Indeed, the Final Office Action fails to address the limitation. Appellants incorporate their arguments from section II.(A.)(1.) here by reference.

3. The Examiner improperly combines the teachings of Bosch with Breitbarth.

Appellants incorporate their arguments from section II.(A.)(2.) here by reference. Tan fails to remedy the deficiencies of Bosch and Breitbarth noted above.

B. Dependent claim 65 is patentable over Tan in view of Bosch, Breitbarth, Ma, and Daraio.

Appellants incorporate their arguments from section II.(B.) here by reference. Tan fails to remedy the deficiencies of Bosch, Breitbart, Ma, and Daraio noted above.

In conclusion, Appellants request favorable action and allowance of the presently pending claims.

Respectfully requested,

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8. CLAIMS APPENDIX

1-27. (Cancelled)

28. (Rejected) A method of utilizing a triggerably releasable delivery system, the method comprising administering to a mucosal membrane of a patient a plurality of nanoparticles containing silica coated with alumina and having a size of about 500 nanometers or less, wherein the alumina provides a site on a surface of the nanoparticles to which is bonded a functional compound, wherein the nanoparticles possess a zeta potential of about 20 millivolts or more, wherein the nanoparticles are contained within a vehicle that further comprises a pH altering material, and wherein the functional compound is released from the surface of the nanoparticles upon exposure to a change in pH.

29. (Cancelled)

30. (Rejected) The method of claim 28, wherein the nanoparticles posses a zeta potential of about 30 millivolts or more.

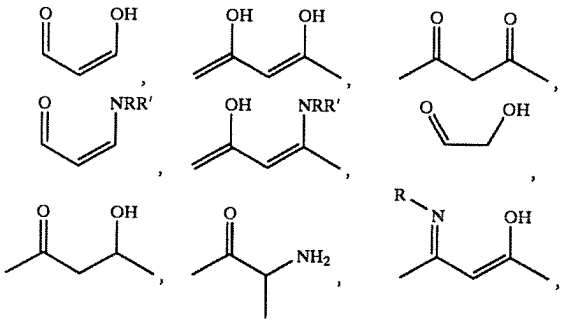
31. (Rejected) The method of claim 28, wherein the nanoparticles posses a zeta potential of about 40 millivolts or more.

32. (Cancelled)

33. (Rejected) The method of claim 28, wherein the functional compound is an anti-microbial agent, anti-viral agent, or a combination thereof.

34. (Rejected) The method of claim 28, wherein the functional compound is a therapeutic agent.

35. (Rejected) The method of claim 28, wherein the functional compound contains a moiety comprising:



or a tautomer thereof, or a functional equivalent thereof, wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group.

36. (Cancelled)

37. (Rejected) The method of claim 28, wherein the vehicle is a liquid.

38. (Rejected) The method of claim 28, wherein the vehicle is a gel.

39. (Cancelled)

40. (Rejected) The method of claim 28, wherein the nanoparticles are located on a substrate prior to administration to the patient.

41. (Cancelled)

42. (Rejected) The method of claim 28, wherein the change in pH involves a change from an acidic to an alkaline pH.

43. (Rejected) The method of claim 28, wherein the change in pH involves a change from an alkaline to an acidic pH.

44. (Rejected) The method of claim 28, wherein the nanoparticles are topically administered.

45. (Cancelled)

46. (Rejected) The method of claim 28, wherein the mucosal membrane is located in the vagina of a female.

47-61. (Cancelled)

62. (Rejected) The method of claim 28, wherein the pH altering material includes an acid.

63. (Rejected) The method of claim 28, wherein the pH altering material includes a base.

64. (Rejected) The method of claim 28, wherein the functional compound contains the following moiety:

65. (Rejected) The method of claim 64, wherein the functional compound includes tetracycline.

66. (Withdrawn) The method of claim 64, wherein the functional compound includes baicaline hydrate, baicalein, daunorubicin, or a combination thereof.

67. (Withdrawn) The method of claim 64, wherein the functional compound includes salicylanilide, salacetamide, salsalate, albofungin, or a combination thereof.

9. EVIDENCE APPENDIX

None

10. RELATED PROCEEDINGS APPENDIX

None